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ORIGINAL ARTICLE

Wilson disease: Health-related quality of life and risk for depression

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Summary
Background: Wilson disease is an autosomal recessive disorder of copper metabolism and requires lifelong medical treatment. Therefore, the analysis of quality of life has gathered more attention. Aims of this study were to examine risk for depression and health-related quality of life in patients suffering from Wilson disease.
Methods: Sixty-eight patients were included in this retrospective cross sectional study. The Personal Health Questionnaire-9 Depression Scale was used to assess depression. The Short Form-36 Health Survey questionnaire was used to assess health-related quality of life.
Results: The Personal Health Questionnaire-9 indicated that 21% (14/68) of patients were at risk for major depressive disorders (scores > 10) and 35% (24/68) were at risk for mild depression (scores 5—9). Women had significantly lower life quality scores than men. Primary neurologic disease manifestation was associated with significantly lower total Short Form-36 and subdimension scores compared with primary hepatic or mixed presentation. Overall, patients with Wilson disease experienced higher quality of life than patients with other chronic liver diseases.
Conclusions: As patients with Wilson disease have a high risk for depressive disorders, active assessment for depression is mandatory. Patients with primary neurological symptoms are at higher risk for reduction of life quality.

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Introduction

Wilson disease (WD) is an autosomal recessive disease of copper metabolism caused by mutations in the WD gene ATP7B, leading to impaired biliary excretion of copper with consecutive toxic copper accumulation in liver and brain [1—3]. Patients develop symptoms either due to hepatic or neurologic dysfunction usually in the second or third decade of life, but symptoms may present later [4]. With medical treatment using chelators (D-penicillamine, trientine) or zinc salts, or liver transplantation in selected indications, a regular life expectancy has become the norm [5—10]. Therefore WD has to be considered as a chronic illness in most cases.

In chronic diseases, analysis of factors influencing quality of life (QoL) has recently gathered more and more attention. In this context, health-related quality of life (HRQL) describes the consequences of health status on physical function, psychological health and social functioning [11]. Different standardized tests have been developed to measure HRQL [12—16]. Widely used questionnaires include the Short Form-36 Health Survey (SF-36) and the MOS SF-36, which was developed in the Medical Outcomes Study (MOS) [17,18]. SF-36 values are available for healthy population [19—21] and populations with a variety of diseases, including chronic liver diseases [22]. QoL in patients with WD has been analyzed in only a few small studies [23—27], which were reviewed recently [28].

Chronic illness is often associated with depression [29]. Reports on small cohorts have indicated an association of depression and WD [25,27,28], but the clinical consequences are unclear. A screening tool, the short version of the Patient Health Questionnaire, with nine questions (PHQ-9), can be used to identify patients with potential depressive disorders, mild to moderate depression, and major depressive illness [30—34]. This one-step questionnaire has not been used previously in WD patients.

The purpose of this study was to measure the QoL in WD patients, identify the risk for depression, and examine potential modifying factors using the SF-36 and PHQ-9 questionnaires.

Methods

We conducted a retrospective cross sectional study.

All patients included had confirmed diagnosis of WD [5,6], attended our tertiary WD care center, and were 18 years of age or older. Patient history was as described previously [35,36]. Patients receiving antipsychotic or antidepressant co-medication and patients who underwent liver transplantation for WD were excluded from the study.

Clinical presentation and laboratory assessments of liver function at the time of diagnosis of Wilson disease were used to classify patients. Patients with elevated liver enzymes or clinical signs of liver cirrhosis were considered symptomatic hepatic. Patients were classified as symptomatic neurologic, depending on the presence or complete absence of neuropsychiatric symptoms evaluated by a chart review at the time of initial diagnosis. Patients were classified as ''mixed'' when both hepatic and neuropsychiatric symptoms were present.

Patients were asked to complete the SF-36 questionnaire version 2.0 [37,38] and the PHQ-9 questionnaire [39], which are both available in German, before their regular medical visit for WD in the outpatient clinic. The PHQ-9 has a maximum of 27 points, and the following cut-offs were adopted: 0—5 = no evidence for depressive disorder, 5—10 = mild/latent depressive changes, and 10—27 = major depressive syndrome [31].

The SF-36 questionnaire contains 36 questions with normalized scores ranging from 0 (low QoL) to 100 (optimal QoL) in eight dimensions: physical function, physical role, body pain, general health, vitality, social functioning, emotional role, and mental health. Dimensions of HRQL, such as general physical health or general mental health, can be calculated separately.

The standardized and total PHQ-9 scores, SF-36 dimension scores, SF-36 physical and mental health summary scores, and total SF-36 score were used in the analyses. These scores were calculated as described previously [17,20,21].

Approach to monitoring and medical therapy

In line with current guidelines, patients generally began chelation treatment when symptomatic. No systematic criteria were used regarding the choice of chelating agents. Patients received zinc salts only when presenting with normal and compensated liver function. Patients with a stable course were seen in the tertiary centers approximately once a year.

Statistical analysis

Statistical analyses were performed with PASW Statistics 18 by IBM™. Comparisons of quantitative variables were performed using the unpaired Mann-Whitney test. The Kruskal-Wallis test was used in the presence of more than two subgroups. Data are presented as mean ± SD. A *P*-value < 0.05 was considered statistically significant.

Results

Patient characteristics

Patient characteristics are given in Table 1, including initial presentation, onset, and medical therapy. In Table 2, the patient characteristics are grouped by different treatment regimens.

Depression

More than half of all patients were at risk for depression or suffered from manifest depression based on the PHQ-9 questionnaire (PHQ-9 scores > 4) (Table 3). Of this group, 21% (14/68) of all patients with WD were at high risk for major depressive disorder (PHQ-9 scores > 9) and 35% (24/68) were at risk for mild depression (PHQ-9 scores from 5—9). Subgroup analysis of the 14 patients with PHQ-9 scores above 9, which were considered at high risk for major depressive syndrome, revealed a high percentage who were initially